REMARKS

Claims 1-25 are pending in the current application. In an Office Action dated February 28, 2007 ("Office Action"), the Examiner withdrew a prior restriction requirement, acknowledged a previously filed information disclosure statement, accepted drawings submitted on March 11, 2004, rejected claims 1-25 under 35 U.S.C. §101, rejected claims 1-25 under 35 U.S.C. §112, first paragraph, and rejected claims 1-25 under 35 U.S.C. §103(a) as being obvious over Yakhini et al., U.S. Patent No. 6,768,820 ("Yakhini") in view of Nagarajan et al., IEEE Transactions On Nanobioscience (2002) Vol. I, No. 2, pp. 78-84 ("Nagarajan"). Applicant's representative gratefully acknowledges the Examiner's withdrawal of the previous restriction requirement, has amended certain of the claims in the above amendment to address certain of the Examiner's rejections, and respectfully traverses the Examiner's 35 U.S.C. §103, 35 U.S.C. §112, and 35 U.S.C. §103(a) rejections of claims 1-25.

First, with regard to the 35 U.S.C. §101 rejections, Applicant's representative notes that, recently, the USPTO has been far more aggressively asserting 35 U.S.C. §101 deficiencies. However, in general, such assertions, as in this case, rely on an Examiner's determination that the result produced by a claimed method is not concrete, tangible, and useful, despite the fact that the claimed method is carefully described as producing a useful and desired result in the application, and that the claimed method is widely accepted as producing a desired and useful result by those skilled in the relevant art. For example, in the current application, the problems associated with background intensity gradients within images of microarrays are described and illustrated in great detail, beginning on line 26 of page 13. For example, Figure 10 shows, as described in the first paragraph on page 15 of the current application, a subregion of an image of a microarray having a rather steep background-intensity gradient along a horizontal direction. The intensities associated with two features 1006 and 1008 in the subregion are identical when the background-intensity gradient is recognized and the pixel intensities correspondingly corrected, but, when the background-intensity gradient is not recognized, as discussed in this paragraph, much different overall feature intensities

are calculated for the two features. As the current application makes clear, the intensities associated with features, in general, represent the signals derived from microarrays that allow for conclusions to be drawn with respect to the molecular components of various solutions resulting from various experiments. When feature intensities are incorrectly computed, the conclusions drawn from microarray data may be inaccurate or false, just as the accuracy, reliability, and precision of most all scientific conclusions depend on the accuracy, reliability, and precision of the data from which the conclusions are made.

In a second paragraph on page 15, Applicant states:

> In order to carry out background subtraction to recover feature signals from a microarray data set, the presence of gradients, such as the gradient illustrated in the subregion of Figure 10, need to be detected and characterized. For a simple linear gradient, as shown in Figure 10, many currently available feature-extraction methods can be used to obtain accurate integrated signal intensities by detecting, quantifying, and correcting for the linear background intensity gradient across the image of the microarray. However, simple gradients represent only a small subset of the different types of intensity gradients observed in the images of microarrays. Complexly shaped manufacturing defects, patterns of contamination, thumbprints and fingerprints, and scratches and abrasions may produce intricately shaped, non-continuous regions of intensity gradients, with varying directions of steepest increase, within the image of a microarray. In many cases, currently available feature-extraction programs have difficulty detecting and correcting for such complex gradients.

Thus, Applicant's representative cannot understand how it is possible to conclude that a method for detecting background-intensity gradients in a microarray data set can possibly be viewed as not being useful, tangible, or concrete. As indicated in the above-quoted passage, many types of microarray defects lead to non-linear background-intensity gradients that cannot be corrected for by currently available techniques. However, such background-intensity gradients distort the feature signals obtained from microarrays, potentially leading to inaccurate or false conclusions drawn from microarray data. Therefore, the ability to detect such background-intensity gradients would seem to be almost axiomatically useful, tangible, and concrete.

In the interest of facilitating prosecution of this application, Applicant's representative has amended the independent claims, as suggested by the Examiner on

page 3 of the Office Action. It is not Applicant's representative's intention to be argumentative, uncooperative, or stubborn. Applicant's representative merely wishes to point out that the seemingly form-based 35 U.S.C. §101 rejections that are currently offered by the USPTO do not appear to be consonant with the USPTO guidelines or with the broad intent and purpose of the patent system, as initially expressed in the U.S. Constitution, as expressed in 35 U.S.C. §1-376, and as expressed in a rather large body of federal case law.

With regard to the Examiner's 35 U.S.C. §112, first paragraph rejections of claims 1-25, Applicant's representative has amended the independent claims to add further limitation to the term "metrics." However, in these rejections, Applicant's representative believes that the Examiner has applied enablement standards from fields such as molecular biology and pharmaceuticals to the very different fields of computing and signal-processing, in which those enablement standards are neither warranted nor appropriate. Applicant's representative appreciates that, in molecular biology and pharmaceuticals, enablement and written-description standards tend to be enforced quite differently than enablement and written-description standards are applied in fields such as electrical engineering, computing, and mechanical inventions. These differences in application of enablement and written-description requirements seem to derive, at least in part, from a perceived lack of predictability in fields such as pharmaceuticals and molecular biology, and from consideration of the generally much more complex environment in which pharmaceutical and molecular-biology inventions are practiced. For example, questions of bioavailability, unintentional biological targets, metabolic effects, and many other phenomena may often conspire to prevent a theoretically effective pharmaceutical from being effective in target biological organisms and, in certain cases, may actually result in the theoretically effective pharmaceutical being deleterious or even toxic.

The claimed embodiments of the current invention are not directed to inherently unpredictable fields, such as molecular biology or pharmaceutical fields or environments. By contrast, the claimed embodiments of the current invention are directed to a computational method for identifying background-intensity gradients within

microarray data sets. The background-intensity gradients may arise from any number of different phenomena, defects, experimental errors, and the characteristics of solutions and microarray surfaces, as intimated in the above-quoted paragraph. For the purposes of the current application, the nature of the causes of the background-intensity gradients are largely irrelevant. Instead, the current application is directed to a computational method for detecting background-intensity gradients regardless of how and why the background-intensity gradients arose. Although the chemistry and molecular biology of some of these effects may indeed be complicated, that chemistry and molecular biology is largely irrelevant.

As the Examiner must surely appreciate, a claim directed to a very precise description of a general computational method, when many other methods falling within the scope of the general computational method may also be used, has very low value to an applicant. Moreover, under U.S. patent law, an applicant has the right to claim an invention as broadly as the patent statutes allow. Moreover, in the current application, Applicant specifically states, beginning on line 18 of page 17, that "[a]lternative convergence metrics are possible, including convergence metrics related to the above-described convergence metrics by constant multipliers, as well as the lengths of other types of mathematical features correlated with background region areas." Furthermore, beginning on line 6 of page 33, Applicant states:

> In the above-described implementation, the annulus with the greatest absolute value of the difference between average and medium pixel intensities is selected to define the convergence metric, but in alternative implementations, an annulus immediately preceding or following the annulus with the greatest difference between the average and median pixel intensities may instead be selected. The selection may also be based on the shape of the plotted differences versus radii graphs, described above with reference to Figures 14 and 15, may be based on the derivatives of that curve, or on a variety of different numerical and computational values based on pixel intensities with annular background regions of increasing radii. As another example, a statistical value, such as the variance or standard deviation of pixel intensities may be used, rather than the difference between the average and median pixel intensities. As discussed above, square background regions of increasing half widths may be employed for square features, and a variety of other different shaped background regions of increasing dimensions may be employed where

> appropriate. As mentioned above, there are an almost limitless number of implementations of a convergence metric computation routine.

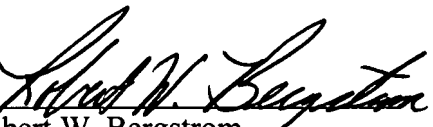
Thus, Applicant clearly contemplated a variety of different convergence metrics. However, the current claims are directed to a well-defined class of background-intensity-gradient identification methods, and not to just any background-intensity-gradient identification method. For example, the currently claimed method identifies background-intensity gradients based on convergence metrics computed for individual features of a microarray data set. In other background-intensity-gradient identification methods, background-intensity gradients may alternatively determined by global metrics and globally-applied procedures, rather than feature-based metrics. As far as Applicant and Applicant's representative know, there are no background-intensity-gradient identification methods in the prior art that rely on convergence metrics computed for features or groups of features within a microarray data set. Thus, in Applicant's respectfully offered opinion, Applicant is entitled to broadly claim background-intensity-gradient identification methods that use feature-based convergence metrics, such as those described in the current application.

With regard to the Examiner's 35 U.S.C. §103(a) rejections, Applicant's representative respectfully points out that neither Yakhini nor Nagarajan are concerned with identifying, or correcting for, background-intensity gradients. Instead, both Yakhini and Nagarajan employ background-correction methods that compute average, local backgrounds for each feature. In essence, both Yakhini and Nagarajan are concerned with computing the magnitude of the background intensity, which is a scaler value generally corresponding to some local, regional, or global average background computed for a microarray data set. By contrast, the current application is directed to identifying background-intensity *gradients*. A gradient is not a scaler value, but is instead a vector quantity expressing the rate of change of the background intensity in a particular direction within a microarray image. The task of computing background-intensity gradients is, in general, far more computationally intensive than computing local, regional, or global average backgrounds. The average backgrounds, as stated above, are scaler values that can generally be computed in a single pass. By contrast, gradients are

directional values, and may require fairly sophisticated, non-local computation to identify, for example, the direction of greatest change, or the steepest gradient, at a given point in a microarray image. While many gradient-identification computational techniques may be possible, Applicant has invented a particularly efficient method for identifying background-intensity gradients using local, feature-based convergence metrics, rather than by using more computationally intensive, global analysis. Yakhini and Nagarajan do not discuss, mention, or suggest problems associated with background-intensity gradients, and neither reference, nor both references in combination, teaches, mentions, or suggests a method for identifying background-intensity gradients. Therefore, neither reference alone, nor both references in combination, can possibly teach the claimed method for identifying background-intensity gradients within a microarray data set.

In Applicant's representative's opinion, all of the claims remaining in the current application are clearly allowable. Favorable consideration and a Notice of Allowance are earnestly solicited.

Respectfully submitted,
Srinka Ghosh
Olympic Patent Works PLLC



Robert W. Bergstrom
Registration No. 39,906

Enclosures:
Postcard
Transmittal in duplicate

Olympic Patent Works PLLC
P.O. Box 4277
Seattle, WA 98194-0277
206.621.1933 telephone
206.621.5302 fax